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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
HOLT, ANDRIAE M	

ART UNIT	PAPER NUMBER
1616	

NOTIFICATION DATE	DELIVERY MODE
12/07/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

ADIPFDD@bipc.com

Office Action Summary	Application No.	Applicant(s)	
	10/031,949	COUARAZE ET AL.	
	Examiner	Art Unit	
	Andriae M. Holt	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3*

10031949 - Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 August 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3-6 and 8-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-6 and 8-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is in response to Applicant's request for reconsideration filed August 28, 2009. Claims 3-6 and 8-18 are pending in the application. Claims 3-6 and 8-18 will presently be examined to the extent they read on the elected subject matter of record.

Status of the Claims

Rejections not reiterated from the previous Office Action are hereby withdrawn. The following rejections are reiterated. They constitute the complete set of rejections presently being applied to the instant application.

The rejection of claims 11-12 under 35 U.S.C. 102(b) as being anticipated by Bhutani (US 4,684,516) **is maintained**.

The rejection of claims 11-12 are rejected under 35 U.S.C. 102(b) as being anticipated by Harrison et al. (US 4,806,361) **is maintained**.

The rejection of claims 3-6 and 8-18 under 35 U.S.C. 103 (a) as being unpatentable over Frost et al. (WO 88/02629) in view of Makino et al. (US 4,983, 399) **is maintained**.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 11-12 are rejected under 35 U.S.C. 102(b) as being anticipated by Bhutani (US 4,684,516).

Bhutani discloses the active ingredient is first coated onto non-pareil beads (neutral microgranules, 62.5% to 91.5% sucrose and the remainder starch) or onto drug crystals or granules. Bhutani discloses these pellets are then divided into several groups and varying amounts of retarding materials are applied to different groups. Bhutani discloses the stabilized pellets are then coated with several layers of disintegrating agent or agents (active agents) and compressed into tablets or pills, after adding a small amount of lubricants or other inert ingredients, if necessary (lubricant of 0 and 1%)(tableting premix). Bhutani discloses that such a compressed tablet, when tested in water or gastric fluid, breaks up quickly thereby releasing the individual pellets in a matter of minutes, whereupon they act as independent pellets releasing their medicine at a predetermined rate (col. 4, lines 11-29). Bhutani teaches the tablet composed of 85% to 98% of the drug-containing, coated, spherical pellets, the remainder being composed of binder and lubricants, preferably between 90% to 100% of the tablet (99 and 100% neutral microgranules). The pellets are predominantly of a size ranging from 12 to 30 mesh, with sizes 16 thru 24 mesh being preferred and they all may be the same size or of different sizes within that range (col. 5, lines 40-47). The 12 to 30 mesh is within the same range as 200 and 400 μm of the instant invention. Bhutani discloses in examples 1, 3, and 4 preparation of tablets using Nonpareil seeds (sugar pellets). Bhutani disclosed in example No. 4, Nonpareil seed (sugar pellets), 30.0

kg., all passing through a No. 30 U.S. mesh screen, 90% passing through a No. 35 U.S. mesh screen, and not over 10% passing through a No. 40 U.S. mesh screen are placed in a 48-inch coating pan. The pan is set in rotation and coating solution is sprayed slowly onto the pellets in order to wet them evenly. Then 400 gm of theophylline anhydrous containing approximately 5% talcum powder is sprinkled on the wetted mass of nonpareil seeds.

These tablets are then coated using conventional coating techniques for improving appearance and acceptability. The coated tablets thus obtained released the active ingredient at a sustained rate over a period of 10 to 12 hours under physiological conditions (col. 11, lines 1-49).

Bhutani meets all the limitations of the claims and thereby anticipates the claims.

Response to Arguments

Applicant's arguments filed August 28, 2009 have been fully considered but they are not persuasive. Applicant argues that Bhutani contains more than 0-1% of other ingredients and that the instant application expressly requires that 99-100% of the formulation is neutral microgranules coated with an active agent. In response to Applicant's arguments, Bhutani discloses that the tablet composition is composed of 85% to 98% of the drug containing, coated, spherical pellets. Bhutani discloses in example 4 that the theophylline anhydrous containing approximately 5% talcum powder was sprinkled on the wetted mass of nonpareil seeds. The talcum powder is used as a binder in the formulation. Applicant's claims a "tableting premix" wherein the neutral microgranules are coated with an active principle and "the active principle mixture

consists essentially of an active principle and an optional binder". As such, the skilled artisan would anticipate that the pellet composition as taught by Bhutani would anticipate the instant claims, especially since Applicant does not indicate the amount of binder that can be used in the formulations. Bhutani discloses more coatings of the theophylline anhydrous coating containing the talcum powder are applied to the nonpareil seed until the theophylline anhydrous powder is used up. Applicant does not indicate only one coating of the active principle mixture is applied to the neutral microgranules. The nonpareil seed pellets coated with the active agent taught by Bhutani anticipates the premix of the instant application in that no lubricant is used in the formulation. The claims remain rejected.

Claims 11-12 are rejected under 35 U.S.C. 102(b) as being anticipated by Harrison et al. (US 4,806,361).

Harrison et al. disclose in col. 6, lines 29-47, the preparation of Nonpareils Coated with Medicament. Harrison et al. disclose that 11 parts of hydroxypropylmethylcellulose were suspended in 111 parts of purified water previously heated to boiling. 440 additional parts of water were then added to the suspension and the whole stirred until a diluted Pharmacoat suspension had formed. Harrison et al. further disclose that 11 parts of 1,2 dihydro-3-cyano-6-methyl-5-(4-pyridinyl)-2(1H)-pyridinone (active agent) were stirred into the Pharmacoat suspension until well dispersed. 200 parts of nonpareils (sugar/starch base: 25-30 mesh) (neutral microgranules) were placed in a coating column or pan and, whilst passing an atomizing

current of warm air there through, the diluted Pharmacoat suspension was gradually added. Harrison et al disclose that after all the Pharmacoat suspension had been added, the passage of the current of warm air was continued until the coated nonpareils were dry.

Harrison et al. meet all the limitations of the claims and thereby anticipate the claims.

Response to Arguments

Applicant's arguments filed August 28, 2009 have been fully considered but they are not persuasive. Applicant argues that Harrison teaches added layers, coatings, and polymers and do not anticipate the presently claimed formulation. In response to Applicant's arguments, Harrison teaches in Preparation A, the 1,2 dihydro-3-cyano-6-methyl-5-(4-pyridinyl)-2(1H)-pyridinone (active agent) were stirred into the Pharmacoat. Pharmacoat is used in the formulation as an adhesive, a binder. Applicant's claims a "tableting premix" wherein the neutral microgranules are coated with an active principle and "the active principle mixture consists essentially of an active principle and an optional binder". As such, the skilled artisan would anticipate that Preparation A as taught by Harrison would anticipate the instant claims, especially since Applicant does not indicate the amount of binder that can be used in the formulations. Harrison does disclose that the Pharmacoat suspension was gradually added until all the Pharmacoat suspension had been added, but does not indicate it was added in layers. In addition, Applicant does not indicate only one coating of the active principle mixture is applied to the neutral microgranules. The Preparation of the Nonpareils Coated with Medicament

taught by Harrison anticipates the premix of the instant application in that no lubricant is used in the formulation. The claims remain rejected.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 3-6 and 8-18 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Frost et al. (WO 88/02629) in view of Makino et al. (US 4,983, 399).

Applicant's Invention

Applicant claims a tablet comprising less than 40 mg/g of active principle attached as a coating to neutral microgranules comprising 62.5 to 91.5 % sucrose and the remainder starch. Applicant claims the tablet includes a compression excipient at less than 1% by weight of the tablet.

Determination of the scope of the content of the prior art (MPEP 2141.01)

Frost et al. (WO 88/02629) teach on page 4, example II, alcohol dissolved Killodone 90 is used as a wetting agent for nonpareil seeds (20 to 30 mesh) in a coating pan with repeated dustings of 2', 3'-didesoxyadenosine (about ten to twenty times) to build up a 2', 3'-didesoxyadenosine-coated nonpareil seed. Frost et al. teach a total adult daily dosage is spread out over three to five administrations per day, or twice daily in the sustained release. Frost et al. teach the tablets comprise from about 2 to about 1000 mg per day, most preferably 10 to 250 mg per administration (page 4, lines 13-18) (40 mg/g active). Frost et al. teach in one embodiment there is a sustained release composition which comprises a plurality of dosage units each having at least two components including 2', 3'-didesoxyadenosine and an outer inert component stable in acidic pH which dissolves in a basic pH. Frost et al. teach tablets of a total weight of 330 mg are produced by mixing and then compressing together in a ratio of 10:1 of the dosage subunits of example II and hydroxypropylmethyl cellulose. Frost et al. teach the sustained release tablet of example VII provides an advantage over the other dosage forms in that the dosage subunits are only gradually exposed to the environment of the gastrointestinal fluids, whereby 2',3'-didesoxyadenosine is introduced into the bloodstream over a prolonged period of time (page 6, lines 3-12). Frost et al. teach the compressed tablet containing the plurality of dosage subunits, the matrix of the tablet disintegrating in the gastrointestinal tract to yield the plurality of dosage subunits (page 2, lines 11-15).

Ascertainment of the difference between the prior art and the claims (MPEP 2141.02)

Frost et al. do not teach the compression force between 10 and 30 kN or the disintegration is less than 15 minutes. It is for this reason Makino et al. is joined as a secondary reference.

The teachings of Makino et al. are incorporated herein by reference and are therefore applied in the instant rejection as discussed above.

Finding of prima facie obviousness
Rationale and Motivation (MPEP 2142-2143)

It would have been obvious to one of ordinary skill in the art at the time of invention to combine the teachings of Frost et al. and Makino et al. and produce tablets that have a disintegration rate less than 15 minutes. One skilled in the art at the time the invention was made would have been motivated to have a disintegration rate less than 15 minutes because Frost et al. teach granules disintegrate rapidly in the gastrointestinal fluids. In addition, Makino et al. teach that use certain excipients and binders, some of which are the same binders that may be incorporated in the matrix taught by Barry, are formulated with the granules have disintegration times ranging from 1 to 30 minutes, the median of which is 15 minutes.

Each of the references is silent as to the compression force ranging between 10 and 30 kN. However the adjustment of the compression force is a matter of routine experimentation and optimization to produce the tablets. One skilled in the art at the time the invention was made would have been motivated to adjust the compression force to range between 10 and 30 kN to produce a tablet with good hardness. The adjustment of particular conventional working conditions (e.g., compression force) is deemed merely a matter of judicious selection and routine optimization which is well

within the purview of the skilled artisan. Accordingly, this type of modification would have been well within the purview of the skilled artisan and no more than an effort to optimize results.

Therefore, the claimed invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made because every element of the invention has been fairly suggested by the cited references.

Response to Arguments

Applicant's arguments filed August 28, 2009 have been fully considered but they are not persuasive. Applicant argues that Frost does not teach a table consisting essentially of neutral microgranules coated with an active principle mixture and only 1% of a compression excipient. In response to Applicant's arguments, Frost teaches formulations of nonpareil seeds coated with 2', 3'-didesoxyadenosine, see example II, page 4. The subunits of example II and hydroxypropylmethylcellulose (excipient) are compressed together to form a tablet at a weight ratio of 10:1. If the weight ratio is 10:1 then it would have been obvious to the skilled artisan that small amounts of hydroxypropylmethylcellulose could be used in the formulation, including a weight of 1%. If the weight of the 2', 3'-didesoxyadenosine component is 10 grams, at a 10:1 weight ratio, the hydroxypropylmethylcellulose would weigh 1 gram, which is 1% of the formulation.

Applicant also argues that Makino does not remedy the deficiencies of Frost. In response to Applicant's arguments, as stated in the previous rejection Makino was relied on to teach disintegration is less than 15 minutes. One skilled in the art at the time

the invention was made would have been motivated to have a disintegration rate less than 15 minutes because Frost et al. teach granules disintegrate rapidly in the gastrointestinal fluids. In addition, Makino et al. teach the use of certain excipients and binders, some of which are the same binders that may be incorporated in the matrix taught by Frost, are formulated with the granules have disintegration times ranging from 1 to 30 minutes, the median of which is 15 minutes. As such, it would have been obvious to the skilled artisan that since the same binders and excipients, which control disintegration rates, were used in the prior art references, the disintegration times of the Frost formulations would fall within the range of 1 to 30 minutes, the median of which is 15 minutes.

None of the claims are allowed.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Andriae M. Holt whose telephone number is (571)272-9328. The examiner can normally be reached on 7:00 am-4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Richter Johann can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Andriae M. Holt
Patent Examiner
Art Unit 1616

/John Pak/
Primary Examiner, Art Unit 1616